

### **Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

#### **Listing of Claims:**

1. (Currently amended) Method for ~~the identification of~~ identifying 5-methylcytosine positions in a sample genomic DNA ~~is characterized by the fact that the following method, said method comprising the steps are conducted of:~~

a) ~~the chemically treating a sample genomic DNA of a~~ obtained from at least one cell, a cell line, a tissue or an individual is chemically treated in such a way that cytosine and 5-methylcytosine react differently and a form products with different base pairing behavior ~~of the two products results in the duplex,~~

b) ~~the same nucleic-acid~~ amplifying, by means of a polymerase reaction, a segment of the sample genomic DNA obtained in step a) is amplified by means of a polymerase reaction,

c) ~~the same nucleic-acid segment of at least one other cell, cell line, tissue or individual or any reference DNA is treated according to performing steps a) and b)~~ on a reference genomic DNA,

d) forming heteroduplexes ~~are formed from the at least two amplified products segments produced in steps b) and c),~~

e) introducing a detectable label ~~is introduced into the heteroduplex~~ heteroduplexes of step d) by means of a reaction, which is specific for non-complementary base pairs, and

f) determining the position of 5-methylcytosine in the sample genomic DNA based on the presence and position of the detectable label.

2. (Original) Method according to claim 1, further characterized in that only positions are used and indicated in which the cytosine methylation is variable between different cells, cell lines, tissues or individuals, for identification of differences in cytosine methylation patterns between different cells, cell lines, tissues and individuals.

3. (Previously presented) Method according to claim 1, further characterized in that disulfite (bisulfite, pyrosulfite) is utilized as the reagent for selective conversion of cytosine to uracil, whereby 5-methylcytosine remains unchanged, in step a) according to claim 1.

4. (Previously presented) Method according to claim 1, further characterized in that genomic DNA of several individuals, tissues, cell lines or cells is amplified jointly in step b) of claim 1.

5. (Previously presented) Method according to claim 1, further characterized in that genomic DNA of several individuals, tissues, cell lines or cells is amplified separately and then treated jointly according to step e) of claim 1.

6. (Currently amended) Method according to claim 1, further characterized in that by formation of heteroduplexes from the DNA of different individuals, tissues, cell lines or cells, erroneous base pairings are produced at the positions at which a 5-methylcytosine was ~~localized~~ located in the genomic DNA.

7. (Currently amended) Method according to claim 1, further characterized in that in step d), by formation of heteroduplexes with a completely methylated reference DNA, erroneous base pairings occur at the positions at which cytosine was ~~found~~ located in the genomic DNA.

8. (Currently amended) Method according to claim 1, further characterized in that at least one of the genomic DNAs is an unmethylated reference DNA and where in step d), by formation of heteroduplexes with a completely demethylated reference DNA, the erroneous base pairings within

the heteroduplex occur at those positions at which 5-methylcytosine was found located in the other genomic DNA.

9. (Currently amended) Method according to claim 6, further characterized in that ~~the erroneous base pairings by means of “chemical mismatch cleavage” (chemical modification at non-complementary positions) lead to a specific or sufficiently selective~~ in step e) the nucleic acid backbone of the heteroduplex is specifically cleaved at these positions cleaved at the non-complementarily base paired positions by enzymatic means.

10. (Currently amended) Method according to claim 6, further characterized in that in step e) the DNA nucleic acid backbone of the heteroduplex is specifically cleaved enzymatically specifically or sufficiently selectively at the erroneous base pairings at the non-complementarily base paired positions by enzymatic means.

11. (Currently amended) Method according to claim 1, further characterized in that ~~DNA fragments are obtained in step e) according to claim 1, whose size infers the cleavage positions and thus the position of methylcytosines and/or the methylation positions that differ between different individuals, tissues, cell lines or cells~~ comprising in e) measurement of the size(s) of the nucleic acids and wherein the location and/or presence of cleaved or labeled positions is therefrom inferred, thereby enabling the identification of the position(s) of methylcytosines differentially methylated between the genomic DNAs.

12. (Currently amended) Method according to claim 11, further characterized in that ~~the~~ analysis of size (molecular weight) of the DNA fragments is conducted by means of mass spectrometry.

13. (Currently amended) Method according to claim 12, further characterized in that the fragments are analyzed by means of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF).

14. (Original) Method according to claim 12, further characterized in that the fragments are analyzed by means of electrospray ionization mass spectrometry (ESI).

15. (Currently amended) Method according to claim 13, further characterized in that the size of the ~~fragments~~ nucleic acids produced in step e) ~~according to claim 1~~ is adapted to the performance capacity of the mass spectrometer.

16. (Currently amended) Method according to claim 15, further characterized in that ~~several~~ in step b) a plurality of PCRs of a gene segment are ~~introduced~~ carried out and ~~the~~ wherein PCR primers of each PCR are ~~set stepwise newly each time so that the fragment size to be expected each time at least in one of these PCRs falls in~~ positioned such that they are sequential, staggered, consecutive or overlapping to other PCR primers used in the plurality of PCRs thereby producing a series of amplificate nucleic acids of different sizes at least one of which is within the mass range detectable by means of mass spectrometry.

17. (Currently amended) Method according to claim 16, further characterized in that one of the PCR primers is positioned newly stepwise by the maximally detectable mass range of the mass spectrometer, relative to the other PCR primer.

18. (Currently amended) Method according to claim 1, further characterized in that in step b) one primer of the PCR polymerase reaction is provided with a chemical function, ~~so that the PCR product enables the polymerase reaction~~ can be to be immobilized on a surface.

19. (Currently amended) Method according to claim 1, further characterized in that the PCR product ~~produced in~~ of step b) is transferred to different reaction vessels and the surfaces of the reaction vessels are chemically treated such that the PCR product can be bound thereon.

20. (Currently amended) Method according to claim 1, further characterized in that PCR products of different individuals that are produced in step c) are transferred into different reaction vessels the surfaces of which are chemically treated such that ~~the PCR product~~ said products can be bound thereon.

21. (Previously presented) Method according to claim 1, further characterized in that an enzyme which forms a complex with a non-complementary base pair is used for step e).

22. (Original) Method according to claim 21, further characterized in that this enzyme is MutS.

23. (Original) Method according to claim 21, further characterized in that the enzyme bears a label, by which a complex can be displayed.

24. (Original) Method according to claim 21, further characterized in that the label is a fluorescence label, a chemiluminescence label, a mass label or a photochemically cleavable mass label.

25. (Currently amended) Method according to claim 1, further characterized in that ~~one compares an amplified DNA sample according to step c) in claim 1, which displays a difference relative to an amplified DNA sample in step b), in a second run of the method itself, with a similar DNA sample according to step b) in claim 1 and with all other DNA samples to be investigated~~ steps (a) to (f) are repeated such that a genomic DNA of step c) is treated according to steps a) and b) and the genomic DNA of a) is treated according to step c).

26. (Currently amended) ~~Method according to claim 1, further characterized in that a preselection of gene segments to be investigated in detail by the mass spectrometer is conducted by means of fluorescence labeling or chemiluminescence labeling of the immobilized DNA strand, the lack of which, after conducting steps d) and e) of claim 1 and a washing step, indicates the presence of methylated cytosines in the investigated genomic DNA segment~~ A method for identification of 5-methylcytosine positions in genomic DNA, characterized by the fact that the following steps are conducted:

a) the genomic DNA of a cell, a cell line, a tissue or an individual is chemically treated in such a way that cytosine and 5-methylcytosine react differently and form products with different base pairing behaviors,

b) a nucleic-acid segment is amplified by a polymerase reaction wherein one primer of the polymerase reaction is fluorescently labeled and provided with a chemical function thereby enabling the immobilization of the amplificate on a surface,

c) the genomic DNA of at least one other cell, cell line, tissue or individual or any reference DNA is treated according to steps a) and amplified by a polymerase reaction such that the same genomic locus as in b) is amplified,

d) heteroduplexes are formed from at-least two amplified products of steps b) and c) wherein erroneous base pairings occur at the positions at which differentially methylated cytosines were located in the genomic DNAs,

e) a chemical mismatch cleavage reaction is carried out wherein the fluorescent label of cleaved nucleic acids is removed by washing,

f) the cleaved nucleic acids are analyzed by mass spectrometry,

g) the presence or presence and position of 5-methylcytosine within the genomic DNA of a) or b) is deduced from the length of the cleaved nucleic acids.

27. ~~(Amended) Method according to one of claims 1 to 25, further characterized in that a preselection is made of the gene segments to be investigated in detail by mass spectrometry by means of a more non-specific variant~~ A method for identification of 5-methylcytosine positions in genomic DNA, characterized by the fact that the following steps are conducted:

a) the genomic DNA of a cell, a cell line, a tissue or an individual is chemically treated in such a way that cytosine and 5-methylcytosine react differently and form products with different base pairing behaviors,

b) a nucleic-acid segment is amplified by a polymerase reaction wherein one primer of the polymerase reaction is fluorescently labeled and provided with a chemical function thereby enabling the immobilization of the amplificate on a surface,

c) the genomic DNA of at least one other cell, cell line, tissue or individual or any reference DNA is treated according to steps a) and amplified by a polymerase reaction such that the same genomic locus as in b) is amplified,

d) heteroduplexes are formed from at-least two amplified products of steps b) and c) wherein erroneous base pairings occur at the positions at which differentially methylated cytosines were located in the genomic DNAs,

e) a detectable label is introduced into the heteroduplex by an enzymatic reaction, which is specific for non-complementary base pairs,

f) either the labeled or non-labeled nucleic acids are analyzed by mass spectrometry,

g) the presence or presence and position of 5-methylcytosine within the genomic DNA of a) or b) is deduced.

28. (Currently amended) Kit for conducting a method according to claim 1, comprising DNA of at least two individuals, tissues, cell lines or cells that are as different as possible, along with reagents, in order to indicate the variable methylation positions.

29. (Original) Kit for conducting the method according to claim 1, comprising completely methylated and/or demethylated DNA and reagents, which are necessary for the detection of methylated cytosines in any DNA sample.